

I. AMENDMENTS

In the Claims

Please enter claims 116 and 164 as re-written below:

Claims 1-115. (Cancelled)

116. (Currently amended) A method for enhancing the delivery of a bioactive agent from the vasculature to a selected tissue in a patient, ~~said method~~ comprising:

- (i) administering said bioactive agent to said patient;
- (ii) administering a vesicle composition to said patient, by ~~continuous~~ intravascular infusion, wherein said vesicle composition comprises, in an aqueous carrier, vesicles comprising lipids, proteins, or polymers and a gas or gaseous precursor; and
- (iii) applying ultrasonic energy to the patient in an amount sufficient to produce cavitation or rupture of said vesicles, and sufficient to increase delivery of said bioactive agent from the vasculature through the vessel wall and into said selected tissue, wherein said bioactive agent is delivered into said selected tissue.

117. (Previously added) A method according to Claim 116 wherein said bioactive agent is administered to said patient at a rate which comprises continuous infusion.

118. (Previously added) A method according to Claim 116 wherein said bioactive agent and said vesicle composition are administered to said patient substantially simultaneously.

119. (Previously added) A method according to Claim 116 further comprising imaging said patient using diagnostic ultrasound imaging.

120. (Previously added) A method according to Claim 116 wherein said vesicles comprise lipids.

121. (Previously added) A method according to Claim 120 wherein said vesicle composition comprises vesicles selected from the group consisting of micelles and liposomes.

122. (Previously added) A method according to Claim 120 wherein said lipids comprise phospholipids.

123. (Previously added) A method according to Claim 122 wherein said phospholipids are selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine and phosphatidic acid.

124. (Previously added) A method according to Claim 123 wherein said phosphatidylcholine is selected from the group consisting of dioleoylphosphatidylcholine, dimyristoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidylcholine.

125. (Previously added) A method according to Claim 124 wherein said phosphatidylcholine comprises dipalmitoylphosphatidylcholine.

126. (Previously added) A method according to Claim 123 wherein said phosphatidylethanolamine is selected from the group consisting of dipalmitoylphosphatidylethanolamine, dioleoylphosphatidylethanolamine, N-succinyldioleoylphosphatidylethanolamine and 1-hexadecyl-2-palmitoylglycerophosphoethanolamine.

127. (Previously added) A method according to Claim 126 wherein said phosphatidylethanol-amine comprises dipalmitoylphosphatidylethanolamine.

128. (Previously added) A method according to Claim 123 wherein said phosphatidic acid comprises dipalmitoylphosphatidic acid.

129. (Previously added) A method according to Claim 120 wherein said lipid further comprises a polymer.

130. (Previously added) A method according to Claim 129 wherein said polymer comprises a hydrophilic polymer.

131. (Previously added) A method according to Claim 130 wherein said hydrophilic polymer comprises polyethylene glycol.

132. (Withdrawn) A method according to Claim 116 wherein said vesicles comprise proteins.

133. (Withdrawn) A method according to Claim 132 wherein said proteins comprise albumin.

134. (Withdrawn) A method according to Claim 116 wherein said vesicles comprise polymers.

135. (Withdrawn) A method according to Claim 134 wherein said polymers comprise synthetic polymers or copolymers which are prepared from monomers selected from the group consisting of poly-lactic acid, poly-lactide, poly-lactide co-glycolide, acrylic acid, methacrylic acid, ethyleneimine, crotonic acid, acrylamide, ethyl acrylate, methyl methacrylate, 2-hydroxyethyl methacrylate, lactic acid, glycolic acid, ϵ -caprolactone, acrolein, cyanoacrylate, bisphenol A, epichlorhydrin, hydroxyalkylacrylates, siloxane, dimethylsiloxane, ethylene oxide, ethylene glycol, hydroxyalkylmethacrylates, N-substituted acrylamides, N-substituted methacrylamides, N-vinyl-2-pyrrolidone, 2,4-pentadiene-1-ol, vinyl acetate, acrylonitrile, styrene, p-amino-styrene, p-aminobenzylstyrene, sodium styrene sulfonate, sodium 2-sulfoxyethyl-methacrylate, vinyl pyridine, aminoethyl methacrylates and 2-methacryloyloxytrimethyl-ammonium chloride.

136. (Withdrawn) A method according to Claim 134 wherein said polymers comprise synthetic polymers or copolymers selected from the group consisting of polyacrylic acid, polyethyleneimine, polymethacrylic acid, polymethylmethacrylate, polysiloxane, polydimethylsiloxane, polylactic acid, poly(ϵ -caprolactone), epoxy resin, poly(ethylene oxide), poly(ethylene glycol), polyamide, polyvinylidene-polyacrylonitrile, polyvinylidene-polyacrylonitrile-polymethylmethacrylate and polystyrene-polyacrylonitrile.

137. (Withdrawn) A method according to Claim 134 wherein said polymers comprise polyvinylidene-polyacrylonitrile copolymer.

138. (Previously added) A method according to Claim 116 wherein said gas comprises a fluorinated gas.

139. (Previously added) A method according to Claim 138 wherein said fluorinated gas is selected from the group consisting of a perfluorocarbon and sulfur hexafluoride.

140. (Previously added) A method according to Claim 139 wherein said fluorinated gas comprises a perfluorocarbon.

141. (Previously added) A method according to Claim 140 wherein said perfluorocarbon gas is selected from the group consisting of perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane and perfluorocyclobutane.

142. (Withdrawn) A method according to Claim 116 wherein said gaseous precursor has a boiling point of greater than about 37°C.

143. (Withdrawn) A method according to Claim 142 wherein said gaseous precursor comprises a fluorinated compound.

144. (Withdrawn) A method according to Claim 143 wherein said fluorinated compound comprises a perfluorocarbon.

145. (Withdrawn) A method according to Claim 144 wherein said perfluorocarbon is selected from the group consisting of perfluoropentane and perfluorohexane.

146. (Previously added) A method according to Claim 116 wherein said vesicle composition is administered to the patient at a rate of from about 1×10^6 to less than about 8×10^6 vesicles/Kg-sec.

147. (Previously added) A method according to Claim 146 wherein said vesicle composition is administered at a rate of from about 1×10^6 to about 7×10^6 vesicles/Kg-sec.

148. (Previously added) A method according to Claim 147 wherein said vesicle composition is administered at a rate of from about 1.5×10^6 to about 6×10^6 vesicles/Kg-sec.

149. (Previously added) A method according to Claim 148 wherein said vesicle composition is administered at a rate of from about 2×10^6 to about 5.5×10^6 vesicles/Kg-sec.

150. (Previously added) A method according to Claim 149 wherein said vesicle composition is administered at a rate of from about 2.5×10^6 to about 5×10^6 vesicles/Kg-sec.

151. (Previously added) A method according to Claim 150 wherein said vesicle composition is administered at a rate of from about 3×10^6 to about 4.5×10^6 vesicles/Kg-sec.

152. (Withdrawn) A method according to Claim 117 wherein said vesicle composition is administered to the patient at a rate of from about 1×10^{-7} to about 3×10^{-3} cc gas/Kg-sec.

153. (Withdrawn) A method according to Claim 152 wherein said vesicle composition is administered at a rate of from about 3×10^{-6} to about 3×10^{-3} cc gas/Kg-sec.

154. (Withdrawn) A method according to Claim 153 wherein said vesicle composition is administered at a rate of from about 4×10^{-6} to about 2×10^{-3} cc gas/Kg-sec.

155. (Withdrawn) A method according to Claim 154 wherein said vesicle composition is administered at a rate of from about 8×10^{-6} to about 2×10^{-3} cc gas/Kg-sec.

156. (Withdrawn) A method according to Claim 155 wherein said vesicle composition is administered at a rate of from about 1×10^{-5} to about 1×10^{-3} cc gas/Kg-sec.

157. (Withdrawn) A method according to Claim 156 wherein said vesicle composition is administered at a rate of from about 4×10^{-5} to about 1×10^{-3} cc gas/Kg-sec.

158. (Withdrawn) A method according to Claim 157 wherein said vesicle composition is administered at a rate of from about 8×10^{-5} to about 1×10^{-3} cc gas/Kg-sec.

159. (Withdrawn) A method according to Claim 158 wherein said vesicle composition is to about 1×10^{-4} to about 9×10^{-4} cc gas/Kg-sec.

160. (Previously added) A method according to Claim 116 wherein said bioactive agent is selected from the group consisting of a diagnostic agent, genetic material, a peptide, a beta-agonist, an anti-asthmatic, a steroid, a cholinergic agent, an anti-cholinergic agent, a 5-lipoxygenase inhibitor, a leukotriene inhibitor, an anti-neoplastic agent, an antibiotic, an anti-tumor drug, a radiation sensitizer, a thrombolytic agent, an anti-histamine, an anti-coagulant, an anti-inflammatory, a hormone, a growth factor, an angiogenic factor and a mitotic inhibitor.

161. (Withdrawn) A method according to Claim 160 wherein said bioactive agent comprises an anti-neoplastic agent.

162. (Withdrawn) A method according to Claim 161 wherein said bioactive agent comprises paclitxel.

163. (Withdrawn) The method of Claim 45 wherein said bioactive agent comprises genetic material selected from the group consisting of a nucleic acid, RNA, DNA, recombinant RNA, recombinant DNA, antisense RNA, antisense DNA, hammerhead RNA, a ribozyme, a hammerhead ribozyme, an antigene nucleic acid, a ribooligonucleotide, a deoxyribooligonucleotide, an antisense ribooligonucleotide, and an antisense deoxyribooligonucleotide.

164. (Currently amended) A method for enhancing the delivery of a bioactive agent from the vasculature to a selected tissue in a patient, ~~said method~~ comprising:

- (i) administering said bioactive agent to said patient;
- (ii) administering an acoustically active composition to said patient, by ~~continuous~~ intravascular infusion; and
- (iii) applying ultrasonic energy to the patient in an amount sufficient to activate said acoustically active composition, and sufficient to increase delivery of said bioactive agent from the vasculature into said selected tissue, wherein said bioactive agent is delivered into said selected tissue and said ultrasound energy has a frequency of from about ~~100 kHz to about 1 MHz~~ 750 kHz to 3 MHz.

165. (Previously added) A method according to Claim 164 wherein said bioactive agent is administered to said patient at a rate which comprises continuous infusion.

166. (Previously added) A method according to Claim 164 wherein said bioactive agent and said acoustically active composition are administered to said patient substantially simultaneously.

167. (Withdrawn) A method according to Claim 164 wherein said tissue comprises neoplastic tissue.

168. (Previously added) A method according to Claim 164 wherein said tissue comprises an area of reduced blood perfusion.

169. (Previously added) A method according to Claim 168 wherein said area of reduced blood perfusion comprises ischemic tissue.

170. (Previously added) A method according to Claim 164 wherein said tissue comprises myocardium.

171. (Previously added) A method according to Claim 164 wherein said tissue comprises glandular tissue.

172. (Previously added) A method according to Claim 171 wherein said glandular tissue comprises the prostate gland.

173. (Previously added) A method according to Claim 164 further comprising imaging said tissue using diagnostic ultrasound imaging.

174. (Previously added) A method according to Claim 164 wherein said bioactive agent comprises an agent selected from the group consisting of a diagnostic agent, genetic material, a peptide, a beta-agonist, an anti-asthmatic, a steroid, a cholinergic agent, an anti-cholinergic agent, a 5-lipoxygenase inhibitor, a leukotriene inhibitor, an anti-neoplastic agent, an antibiotic, an anti-tumor drug, a radiation sensitizer, a thrombolytic agent, an anti-histamine, an anti-coagulant, an anti-inflammatory, a hormone, a growth factor, an angiogenic factor and a mitotic inhibitor.

175. (Withdrawn) A method according to Claim 164 wherein said bioactive agent comprises an anti-neoplastic agent.

176. (Withdrawn) A method according to Claim 175 wherein said bioactive agent comprises paclitaxel.

177. (Withdrawn) A method according to Claim 173 wherein the bioactive agent comprises genetic material selected from the group consisting of a nucleic acid, RNA, DNA, recombinant RNA, recombinant DNA, antisense RNA, antisense DNA, hammerhead RNA, a ribozyme, a hammerhead ribozyme, an antigene nucleic acid, a ribooligonucleotide, a deoxyribooligonucleotide, an antisense ribooligonucleotide, and an antisense deoxyribooligonucleotide.

178. (Previously added) A method according to Claim 174 wherein said acoustically active composition and bioactive agent are administered prior to said application of ultrasound energy.

179. (Previously added) A method according to Claim 174 wherein said acoustically active composition and bioactive agent are administered at about the same time as said application of ultrasound energy.

180. (Previously added) A method according to Claim 174 further comprising applying radiation energy to said tissue.

181. (Previously added) A method according to Claim 179 wherein said acoustically active composition and bioactive agent are administered prior to said application of radiation energy.

182. (Previously added) A method according to Claim 180 wherein said acoustically active composition and bioactive agent are administered at about the same time as said application of radiation energy.

183. (Previously added) A method according to Claim 178 wherein said acoustically active composition and bioactive agent are administered from about 1 minute to about 8 hours prior to said application of ultrasound energy.

184. (Previously added) A method according to Claim 181 wherein said acoustically active composition and bioactive agent are administered from about 1 minute to about 8 hours prior to said application of radiation energy.